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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,746	04/18/2001	Akihiko Sano	0020-4828P	5150

2292 7590 12/30/2002

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EXAMINER	
BENNETT, RACHEL M	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,746	SANO ET AL.	
	Examiner	Art Unit	
	Rachel M. Bennett	1615	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The examiner acknowledges receipt of Amendment B filed 10/4/02.

Specification

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-6, 8-18 are rejected under 35 U.S.C. 103(a) as being obvious over Fujioka et al. (US 5851547) in further view of Fujioka et al. (US 4985253).

Fujioka discloses a drug formulation for producing sustained therapeutic efficacy, which releases at least one water-soluble drug over a prolonged period of time at a substantially constant rate wherein the drug formulation comprises (a) a non-disintegrating inner layer comprised of a biocompatible material that contains at least one uniformly dispersed water soluble drug; and (b) an outer layer comprised of a biocompatible material that surrounds the circumference of the said inner layer, is impermeable to water, and is capable of controlling the swelling of the inner layer; wherein the ratio of the axial length of the drug formulation to the cross-sectional diameter of the inner layer is one or more and wherein one or both ends of the inner layer are open so as to come into direct contact with the external environment (see abstract, claims and figures). The release rate of water-soluble drug is controlled through control of water infiltration. The outer layer material is not critical as long as it is biocompatible, is impermeable to water, and can control the swelling of the inner layer. Hydrophobic polymers are typically

used for this purpose. The non-biodegradable polymers may be exemplified by, but not limited to silicones, polyethylenes or polypropylenes. The inner layer material may be either biodegradable or non-biodegradable (see cols. 5 and 6). Any water soluble drug by be used that is not soluble nor diffusible to the outer layer. Drugs include peptides, proteins, glycoproteins, polysaccharides, nucleic acids, antibiotics, adrimycin, mitomycins, and daunorubicin (see cols. 6 and 7). The inner layer may contain a swelling agent such as sodium chloride, amino acids and glycine. The drug formulation may have a rod-shaped (see col. 7 lines 46-52). The reference does not explicitly state polyethylene glycol as the water-soluble substance.

Fujioka discloses a sustained release composition which comprises a silicone elastomer, a pharmaceutical substance and optionally albumin. The pharmaceutical substance may be peptides, proteins, sugars proteins or polysaccharides (see abstract and col. 2). The release rate of the pharmaceutical substance from the silicone elastomer can be controlled by incorporating a mixing agent such as polyethylene glycol (see col. 3).

Absent unexpected results, it is the position of the examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Fujioka ('547) by using polyethylene glycol in the inner layer because Fujioka ('253) teaches polyethylene glycol may be added to the silicone elastomer in order to control the release rate of the pharmaceutical substance. Therefore, one of ordinary skill in the art would expect to achieve the desired constant release rate of the pharmaceutical using polyethylene glycol in the inner layer.

3. Claims 1-3, 5-7, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takada Kanji (JP 7330581).

Kanji discloses an implantable sustained release immunosuppressive drug comprising 1 to 200 parts by weight of a nonionic surfactant and 0.1 to 100 parts by weight of a fat-soluble immunosuppressive agent combined with 100 parts by weight of a bioabsorbable aliphatic polyester. When implanted in such a manner that it is brought into intimate contact with a lymph duct, the sustained release preparation can effectively transfer the immunosuppressive agent in the preparation into the lymph duct according to a desired sustained release profile (see abstract). The matrix comprises an active agent, a bioabsorbable aliphatic polyester as a base along with a nonionic surfactant, to facilitate the absorption. The implantable sustained release preparation is molded into a shape adapted to a specific organ, the molded article allows effective transfer of the agent into the lymphatic system and also allows control of the duration of sustained release. The non-ionic surfactants include glycerin fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyethylene glycol fatty acid esters, and polyoxyethylene. Examples of immunosuppressive agents include cyclosporin, azathioprine and prednisolone. Although the shape of the implant is not specifically restricted, the implants in the form of a plate, half-cylinder, or film are preferred. Kanji does not specifically disclose the sustained release preparation to be in the form of a rod preparation.

Absent unexpected results, it is the position of the examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Kanji by molding the shape of the implant to be a rod preparation because Kanji teaches the preparation may be any shaped that allows the drug to be implanted in direct contact with the desired site.

Response to Arguments

4. Applicant's arguments filed 10/4/02 have been fully considered but they are not persuasive.

Applicants' argue the drug formulation of Fujioka '547 uses water-soluble drugs. In contrast the sustained release preparation of the instant invention uses a lipophilic drug. Applicants state in the process, because of the great solubility of the water-soluble drug in water, channel formulation immediately occurs upon penetration of water into the inside of the formulation, and this immediate channel formation drives the process. On the other hand, solubility of lipophilic drugs is poor in water, and therefore, the channel formation in the formulation would occur much slower than that in water-soluble formulations. The examiner refers to the instant claims, specifically claims 1 and 10, wherein a lipophilic drug and a water soluble drug are claimed. Thus, Fujioka '547 discloses both a lipophilic and a water soluble drug (see col. 6 lines 35- col. 7 lines 1-6). Furthermore, Fujioka '547 discloses the drug formulation may contain two or more drugs depending on the disease and method of application (see col. 7 lines 7-9) and the drug release form the drug formulation can be adjusted or modulated by a number of techniques such as modifying the type of outer layer material and/or adjusting the outer layer thickness functions to alter the pressure applied to the inner layer (see col. 9, lines 11-17). Lastly, Fujioka '547 states precise control over a broad range is possible because the drug release rate and/or inner layer swelling rate can be varied by varying the drug content of the inner layer and the size and shape of the drug particles and through additive selection. Therefore, the rejection is maintained.

Applicants also argue Kannji '581 fails to teach the ingredients are dispersed in a state of solid. The examiner refers to Kannji '581, pages 7-8, wherein Kannji discloses a molded implantable sustained release immunosuppressive drug and a nonionic surfactant combined with a bioabsorbable aliphatic polyester. The matrix comprises a fat-soluble immunosuppressive agent and a bioabsorbable aliphatic polyester as a base along with an nonionic surfactant further added thereto, and is also characterized in that it is an implantable sustained release preparation molded into a shape adapted to a specific organ. Therefore, it is the position of the examiner the Kannji reference teaches the ingredients dispersed in a state of solid as claimed by Applicants. Thus, the rejection is maintained.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 309-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

R. Bennett
December 27, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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